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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/056,806	04/08/1998	ARNO N VERMEULEN	I/97272	5753

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	09/056,806	VERMEULEN ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,13-15,19,27,28,30 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,13-15,19,27,28,30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3-1-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: for drawing objections see attached as noted 6-9-99 via draftsman.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-25-04 has been entered.

Response to Amendment

2. The amendment filed 5-25-04 has been entered into the record and has been fully considered.

3. Claims 1-5, 13-15, 19, 27-28, 30 and 32 are pending.

4. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

5. As a result of Applicant's amendment, all rejections not reiterated herein are withdrawn.

Claim Objections

6. Claims 1-5, 13-15, 19, 27-28, 30 and 32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The phrase "in its natjve form" should be preceded by "is".

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 13-15, 19, 27-28, 30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment to the claims introduces the new limitation "in its native form." The amendment notes that support for the limitation may be found in the specification for example at pp. 23-24 (see response, p. 6, first paragraph). However, pp. 23-24 of the specification denote various experimental steps in the preparation of sporozoite proteins. These steps include fractionation, and detergent extraction that are deemed as changing the proteins from their native form. In particular, reducing conditions separate whole cell proteins via reduction of chemical bonds that hold proteins in their native form. Note particularly that the whole cells are separated into various protein fractions, pp. 28-33. Hence, the solubilized proteins are not deemed to be in native form and the recitation is not apparently supported by the specification as originally filed.

Applicant's amendment to the claims introduces the new limitation "and a pharmaceutically acceptable carrier." The amendment fails to note where support for the limitation may be found in the specification and the Examiner has

been unable to garner such support from the specification as filed. Hence, the recitation constitutes new matter absent support from the specification as originally filed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any

inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-5, 13-15, 19, 27, 28, 30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by EP0382531, Gurnett, 16.08.90., or in the alternative, under 35 U.S.C. 103(a) as obvious over EP0382531, Gurnett, 16.08.90.

Applicants amendment of 3-21-02 introduces the limitation wherein the extract is of total Eimeria sporozoites. Applicant's specification at pp. 23 discloses the purification of sporozoites via 0.4% taurocholate and purification via nylon wool passage followed by Triton X-114 detergent extraction. Applicant's argue that the amendment distinguishes the composition of claim 1 in that the composition of Gurnett is prepared via a different procedure and is of a detergent extract of sporozoite lysates. Applicants thus conclude that Gurnett does not anticipate the claimed invention.

Applicant's arguments filed 3-21-02 have been fully considered but are not persuasive. Gurnett teaches at pp. 4, lines 24-33, sporozoite purification from pelleted sporocysts via excysting solution of .25% trypsin, 4% taurodeoxycholic acid and 10 mM MgCl2 with incubation at 41 degrees Celsius for about 60 minutes. The released sporozoites are then collected by centrifugation and

washed in PBS, resuspended in Percol and centrifuged again followed by washing in PBS and collection via centrifugation. The sporozoites were then lysed by sonication in water and subjected to either Triton X-114 extraction with or without lipase, see in particular p. 5, line 2 and lines 12-40. Thus, the purification steps of sporozoites are similar and result in the same composition of purified sporozoites, with the exception that the Gurnett reference sonicates the sporozoites prior to Triton extraction whereas the instant application extracts the purified sporozoites without prior sonication. The prior art teaches a hydrophilic phase of a tertoctylphenoxypoly (ethoxyethanol) (triton x-114) extract of Eimeria oocysts, sporulated oocysts and sporozoites. The reference teaches that membrane bound proteins may partition into the hydrophilic phase upon lipase treatment and that such a composition is immunoprotective. Thus, the reference teaches the elements of non-membrane bound (hydrophilic) proteins but also teaches the addition by lipase treatment of particular membrane bound proteins separated from the membrane via lipase treatment. While, the Gurnett reference uses different steps to arrive at the composition there is no apparent step which serves to remove sporozoite proteins prior to the Triton X-114 extraction. Thus, even though the Gurnett reference teaches extraction of sporozoite lysates, this step is not deemed to materially change the components of the lysates from "total" sporozoites as newly claimed. The Gurnett lysates are of total sporozoites and all constituents are contained in the Triton extraction. In other words, simply because the Gurnett reference teaches the extraction step upon lysed sporozoites does not negate that all total proteins are provided to the extraction

as claimed. For there to be a difference between the prior art product and applicants product as newly claimed there must be some distinguishable difference in the composition and not the method by which it is prepared. There is no evidence to conclude that preparations of total sporozoites either with or without the lysing step via sonication would change the material product and the Patent Office has insufficient resources to test whether or not the sonication step results in any material difference of the product claimed from the prior art. Thus, the burden shifts to applicant to show unobvious difference. The Gurnett reference teaches the immunoprotective nature of the compositions so prepared and which correlate to instant claims. It is noted that the molecular weight determination of the four major glycolipid linked proteins from E. tenella sporozoites prepared via such methods as demonstrated in Examples 5 and 6 (see also Table II) reveal that the proteins which may be isolated either in the hydrophilic fraction (when lipase is added prior to phase separation) or the hydrophobic fraction (when lipase is added after phase separation) share the desired molecular weight characteristics of applicants claims. As the evidence shows that the disclosed proteins may be isolated from either the hydrophilic phase of a triton X-114 detergent extraction with lipase, or the hydrophobic phase of a triton X-114 detergent extraction, the disclosed peptide compositions of Gurnett cannot be distinguished from the compositions and vaccines claimed as the preparations are both originated from total sporozoite protein. The Gurnett preparation is protective against Eimeria coccidiosis. The Gurnett reference teaches the vaccine compositions for vaccination (immunization,

protection) with carriers, and with adjuvant, see in particular p. 3, line 40, p. 5, lines 46-48 and p. 7, lines 27-45. For immobilization or labeled compositions as in claim 19, see in particular Examples 1-12.

As in MPEP 2111.03, Applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte,* 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also *Ex parte Hoffman,* 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989).

Applicants amendment of 5-25-04 provides new limitations as to "a vaccine composition". This recitation is deemed to be one of intended use as the recitation fails to impart any particular structural or functional limitations to the claim and therefore the recitation is non-limiting as to the comprised components. The amendment further provides that the composition comprises "a pharmaceutically acceptable carrier." Gurnett teaches at p. 14, Example 12, the purified glycolipid linked protein immunogen, from Example 8 in 0.1% SDS, 0.1 ml/bird. This immunization was effective to provide protection against disease as measured via absence of severe lesion development in birds after normally virulent infection, see also p. 15, first paragraph. Gurnett futher notes in claim 13 the composition of Eimeria immunogen in a physiologically acceptable medium. Hence, Gurnett teaches the composition in a pharmaceutically acceptable carrier. The amendment further requires that the at least one protein or antigenic fragment is in its native form. Gurnett notes that, " Poultry are administered in immunizing dosage of one or more of the native or recombinant

derived Eimeria membrane associated immunogens described above and as noted above with both lipase treated and non-lipase treated compositions, see in particular p. 7, lines 27-30 and pp. 3-7. Nevertheless, as noted above the steps of Gurnett mirror the steps of instant application. Both use sporozoite starting material with subsequent fractionation and purification steps including contact with detergent Triton-X114. Hence, there is no perceived structural difference between the form of Gurnett, the form of the instantly isolated composition and the native form of the protein. As noted above, the burden is shifted to Applicants to show that the recitation imparts a structural distinction to instant claims.

The amendment of 5-20-04 further traverses rejection via an analysis of the Gurnett application as argued at pp. 6-7 of the response. This traversal further points to the Gurnett, Mol. & Biochem. Parasit., 1990 publication submitted 3-1-04. Applicants conclude that only the 26kDa protein was used in the vaccination trial of Example 12 and that the Gurnett application lacks any disclosure of using proteins that are not glycolipid linked or not hydrophobic in a vaccine.

Applicant's arguments filed 5-25-04 have been fully considered but they are not persuasive. First, the Examiner notes that Applicants conclusion that only the 26kDa protein was used in the vaccination of Example 12 is incorrect. Example 12 notes immunization with, "0.01 to 100 ng of the purified glycolipid linked protein immunogen, from Example 8 in 0.1% SDS, 0.1 ml/bird." Review of Example 8 notes that, "several fractions were pooled, acetone precipitated and

were used to immunize chickens, see Example 11, or submitted for sequence analysis, see Example 10. Here it appears that the Gurnett applicantion makes an obvious typographical error in that Examples 10 provides for the Production of Antibody against purified glycolipin linked protein, Example 11 notes Protein sequenceing and Example 12 notes Induction of protection to challenge with E. tenella glycolipid linked protein immunogens. Table 4 further notes protectio of chickens against coccidiosis with glycolipid linked protein of 26 kD. These teachings cannot be negated by Gurnetts typographical errors to Example numbers. While it is true that Gurnett provides data directed to protection with 26kDa protein the teachings are not so limited. Secondly, as noted above, the vaccine recitation does not receive patentable weight to the compositions. Gurnett teaches multiple compositions as noted throughout Examples 1-12 which each may be evaluated with respect to the claim. As noted above Gurnett teaches preparations of whole sporozoites and hence contain both glycolipid linked and non-glycolipid linked proteins. Third, Applicants reference to the Gurnett, Mol. & Biochem. Parasit. 1990 publication is unclear. Applicants apparently assert that the article lacks discussion of a vaccine and only discloses an antiserum against the detergent phase proteins (hydrophobic proteins), the TX114B antiserum. Yet the rejection was not set forth on the basis of the Mol. & Biochem. Parasit. Reference and Applicants provide no arguments as to how such evidence would be effective to remove the rejection of record or prove unobvious distinction over the compositions of EP0382531.

Applicants argue that the 26kDa protein is hydrophobic in its native form and is only rendered hydrophilic via lipase treatment. Hence Applicants assert that the application fails to suitably teach vaccination using a protein or antigenic fragment in its native form. Applicants assert that antigenicity is not immunogenicity. Applicants argue that Gurnett fails to teach or suggest inclusion of a protein that is hydrophilic in its native form in a vaccine use of such a proteins as an immunological reagent or in a test kit or to enable a vaccine incorporation such a protein via lipase treatment.

As noted above Gurnett teaches both preparations, i.e., with and without lipase treatment. Further, Gurnett is not required to teach vaccination using the noted compositions. Nevertheless, Gurnett notes that, " Poultry are administered in immunizing dosage of one or more of the native or recombinant derived Eimeria membrane associated immunogens described above and as noted above with both lipase treated and non-lipase treated compositions, see in particular p. 7, lines 27-30 and pp. 3-7. In response to Applicants assertion that antigenicity is not immunogenicity, Janeway, Charles et al., Immunobiology: the immune system in health and disease, Current Biology Ltd., 1997, p. G:2 notes that, "Antigens are molecules that react with antibodies. Their name arises from their ability to generate antibodies. However, some antigens do not, by themselves, elicit antibody production; only those antigens that can induce antibody production are called immunogens." Hence, Applicant is correct that not all antigens are immunogens. Yet here, the claims are drawn to proteins or antigenic fragments. Claim 19 is distinghuished as an immunological reagent

and not an "immunogen" per say. Thus, there appears to be no uncommonplace where the Gurnett peptides identified as immunogens, see in particular Title, could not be considered as proteins or antigenic fragments. Distinction here is not made. As noted above and in contrast to Applicants assertion the Gurnett reference teaches lipase treated and non-lipase treated Eimeria preparations with proteins present in the hydrophilic phase of a tertoctylphenoxypoly (ethoxyethanol) (TX114) extract and that has a molecular mass of about 26-30 kDa under reducing conditions.

3. Claims 14 and 28 stand rejected as set forth in Paper No. 16, mailed 9-5-01, under 35 U.S.C. 103(a) as being unpatentable over EP0382531, Gurnett et al., 16.08.90, MacKenzie et al., US4,981,684, Jan. 1, 1991 and Estrada et al., US 5,597,807, Jan. 28, 1997.

Applicant's arguments are believed to be essentially as above, in particular applicants argue that if the independent claims are nonobvious that the dependent claims are nonobvious.

Applicant's arguments filed 2-21-02 and 3-21-02 have been fully considered but are not persuasive. The base claim appears properly rejected absent evidence that the introduction of the additional steps would materially change the characteristics of the claimed invention. It is noted that the Gurnett preparation is useful for vaccination purposes as is claimed. Thus, for the aforementioned reasons the rejection is maintained.

Gurnett et al., is set forth above and teaches the composition of claim 1 and vaccine compositions with carrier and adjuvant.

Gurnett et al., fail to teach the composition wherein the adjuvant is Quil A.

MacKenzie et al., teach as of 1991 the knowledge of one of skill in the art who recognized the use of adjuvant complexes, specifically where the glycoside is Quil A (Quillaja saponin) for use in the formulation of vaccines suitable for immunization against pathogens including Eimeria, see in particular Abstract, column 2, lines 43-44 and column 3, line 47.

Estrada et al., similarly teach that as of 1-28-97 (prior to applicants invention) that Quillaja saponins, (Quil A) are especially advantageous to the promotion and production of isoform specific immunoglobulin, specifically IgG and IgA antibodies which enhance both humoral ans secretory immune responses in invertebrates, see in particular columns 5-6, General Methods. Estrada also particularly points to the use of Quillaja saponins in Eimeria vaccine preparations, see in particular column 6, line 30.

Thus, it would have been prima facie obvious to one of skill in the art at the time of invention to modify the vaccine of Gurnett et al., using the adjuvant Quil A to provide for the advantageous and superior benefits of stimulating IgG and IgA antibodies against the Eimeria antigens for the purpose of producing protective immunity in mammalian hosts. The skilled artisan would have motivation to do so and would have expected positive results given the teachings of Gurnett, MacKenzie and Estrada as set forth above and as exemplified in the various references. Thus, the cumulative reference teachings render the claimed invention obvious to the skilled artisan.

Applicants argue in the response of 5-25-04 that for at least the reasons

as noted above the Gurnett application fails to teach or suggest the vaccine including the hydrophilic proteisn of the claimed invention and that neither Estrada or Mackenzie rectify such teachings.

Applicant's arguments filed 5-25-04 have been fully considered but are not persuasive for the reasons set forth above. Gurnett teaches the same hydrophilic preparation and further notes compositions, use as an immunogen and vaccine preparation and further demonstrates the induction of antibody responses as well as protection in chickens as noted above. The compositions include preparations comprising a pharmaceutically acceptable carrer and at least one protein or antigenic fragment in its native form that is present in the hydrophilic phase of a tertoctylphenoxypoly (ethoxyethanol) extract of Eimeria sporozoites and has mass of about 26-30 kDa under reducing conditions. Thus, the references render obvious the claimed invention.

Status of Claims

4. No claims are allowed.

Conclusion

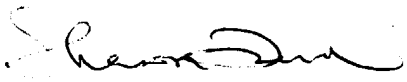
5. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information

for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.



Sharon L. Turner, Ph.D.
July 30, 2004

SHARON L. TURNER, PH.D.
PATENT EXAMINER